

# Isomers and Isomerism

Lec:1

Isomers

- Isomers are different compounds with the same molecular formula. They have the same numbers of same kinds of atoms, but they differ in the way that those atoms are attached to one another, or how they are oriented in space, (Greek: isos= equal; meros=part)

## Isomerism

The presence of two or more compounds which have the same molecular formula is known as Isomerism

1. **Structural isomers:** differ in the way the atoms are connected to each other. Structural isomers having:

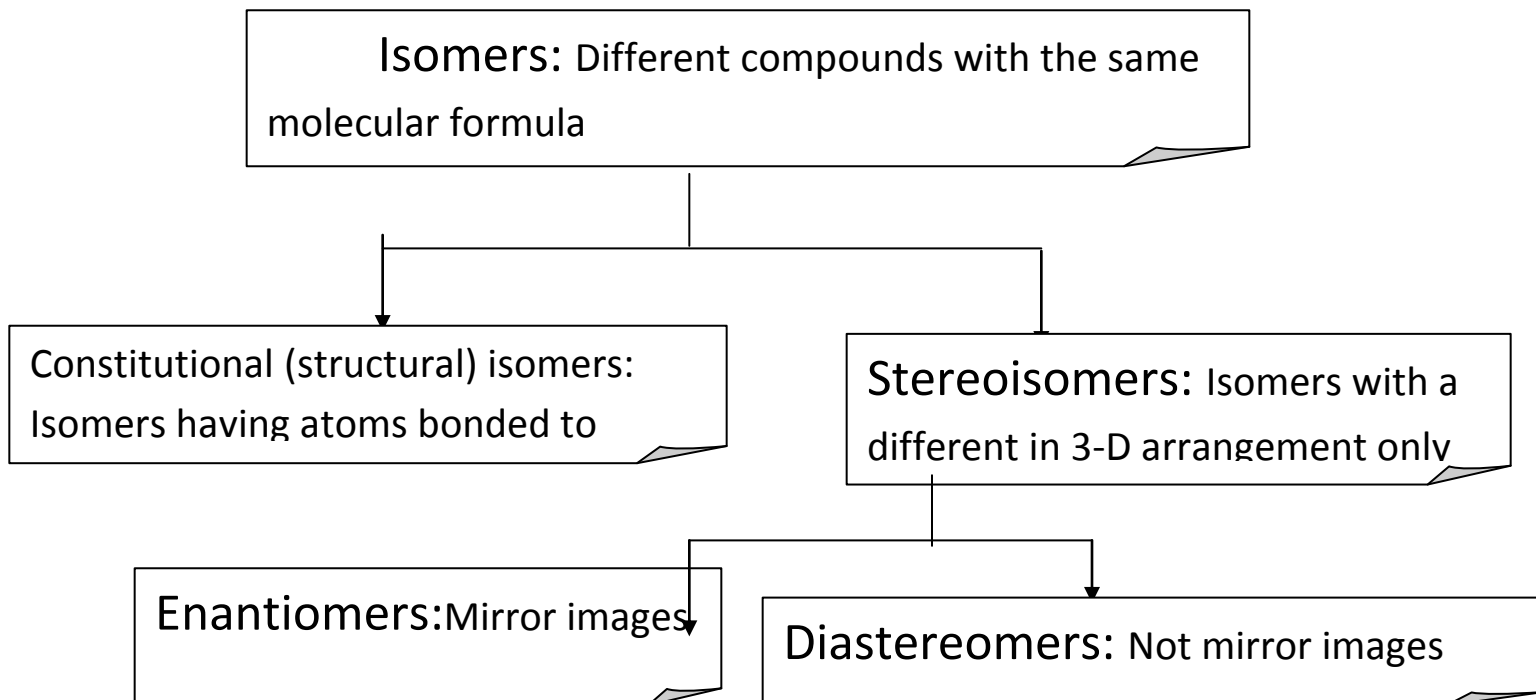
\*different IUPAC names.

\*The same or different functional groups.

\*Different physical properties, so they are separable by physical techniques such as distillation and

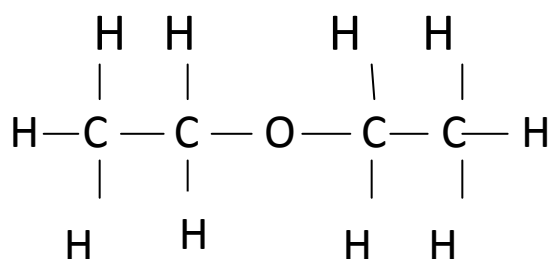
\*Different chemical properties. They behave differently or give different products in chemical reaction.

2. **Stereoisomers** : differ only in the way atoms are oriented in space.

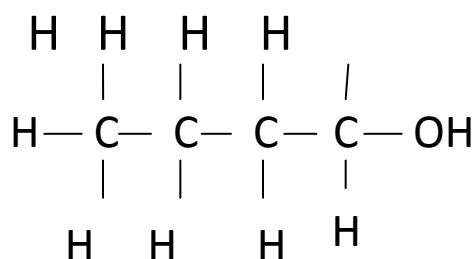


### 1. Structural isomers:

**a-Functional group isomers:** Two or more compounds in which each belongs to a different family of compounds are known as **functional group isomers**. Diethyl ether and n-butyl alcohol are functional-group isomers. Each isomer belongs to a different family of compounds .



Diethyl ether



n- Butyl alcohol

Propionic acid and methyl acetate represent another example of functional group isomerism .

In both examples of functional group isomerism, the atoms are arranged in different ways. This leads to different structural

formulas and therefore different physical and chemical properties. The differences in physical properties are due to significant differences in intermolecular forces between, say molecules of n-butyl alcohol (b.p.117°C, soluble in water at room temperature, Sp.gr 0.81) as opposed to those forces between molecules of diethyl ether (b.p 35°C, slightly soluble in water at room temperature, Sp.gr. 0.71).

functional- group isomers show different chemical properties. For example diethyl ether dose not react with sodium, whereas n-butyl alcohol reacts with sodium to give the corresponding alkoxide and hydrogen .

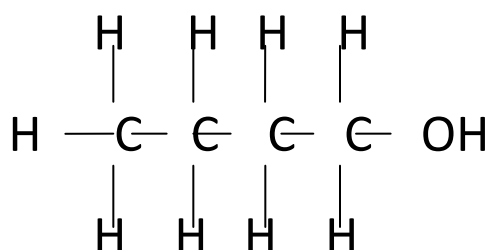


**B- positional isomers:** two or more compounds that belong to the same chemical family, where the same functional group occupies a different position in each molecule are called positional isomers.

For example, compound (a) n-butyl alcohol, b.p 117°C, soluble in water at room temperature, Sp.gr. 0.81 is an isomer of compound (b) sec-butyl alcohol ,(b. p.110°,very soluble in water at room temperature, Sp.gr.0.81) because in (a) the hydroxyl group is bonded to the end carbon,whereas in (b)the hydroxyl group is bounded to the carbon next to the end carbon.

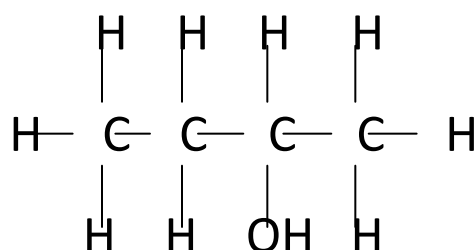
n-Butyl alcohol

a



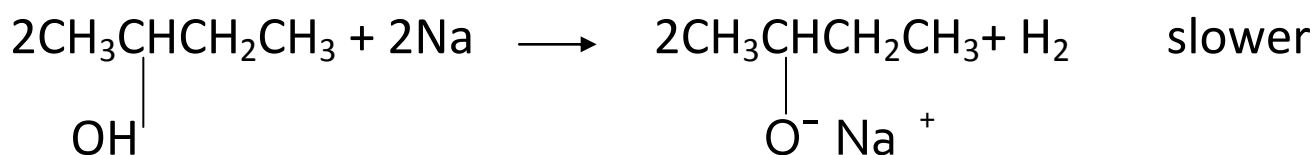
Sec-Butyl alcohol

b

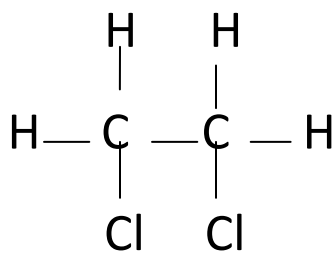


Note that the physical properties shown by positional isomers are not as significantly different as those properties of functional – group isomers.

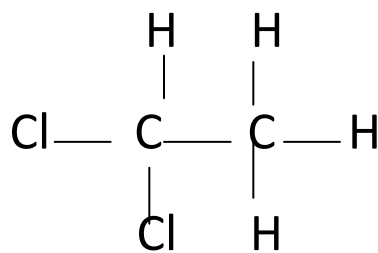
This is because positional isomers contain the same functional group, so their intermolecular forces are similar. Thus each isomer will show somewhat similar physical properties . These same relationships hold for the chemical properties of isomers. Since positional isomerism contain the same functional group these isomers display similar chemical properties. For example, each isomer reacts with sodium in a similar way but at different rates.



Let us consider another illustration of positional isomers. Isomer (c) has one chlorine bonded to each carbon, while isomer (d) has one carbon and two chlorines bonded to the other.

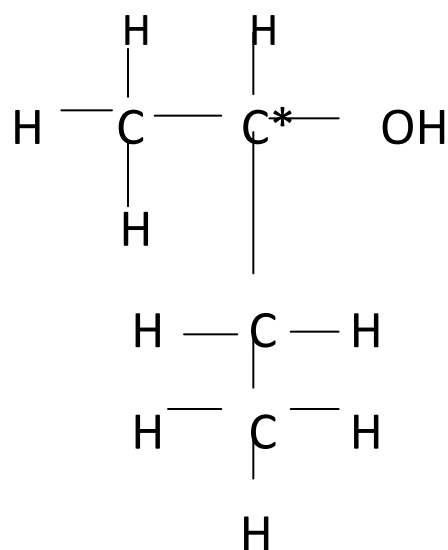


(c)

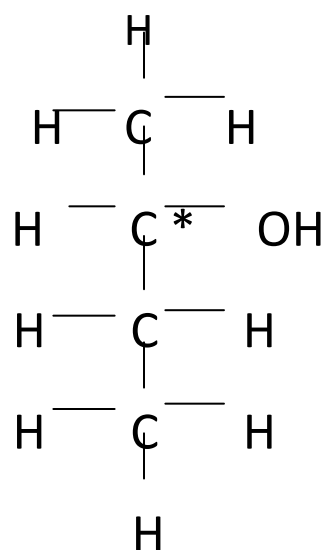


(d)

If two structures have the same atomic surrounding, the structures represent the same compound. Thus both (e) and (f) are identical to compound (b).



( e )



(f)

Each starred carbon has bonded to it one H, one OH, one CH<sub>3</sub>, and one C<sub>2</sub>H<sub>5</sub> group.

**2) Stereoisomers :** These differ from structural isomers, in that structural isomers have different structural formulas, while stereoisomers have the same general structural formula but different orientations in space.

There are different kind of stereoisomers:

a. **Optical isomers** (e.g. enantiomers).

- b. **Geometrical isomers** (cis, trans isomers).
- c. **Conformational isomers** (conformers).

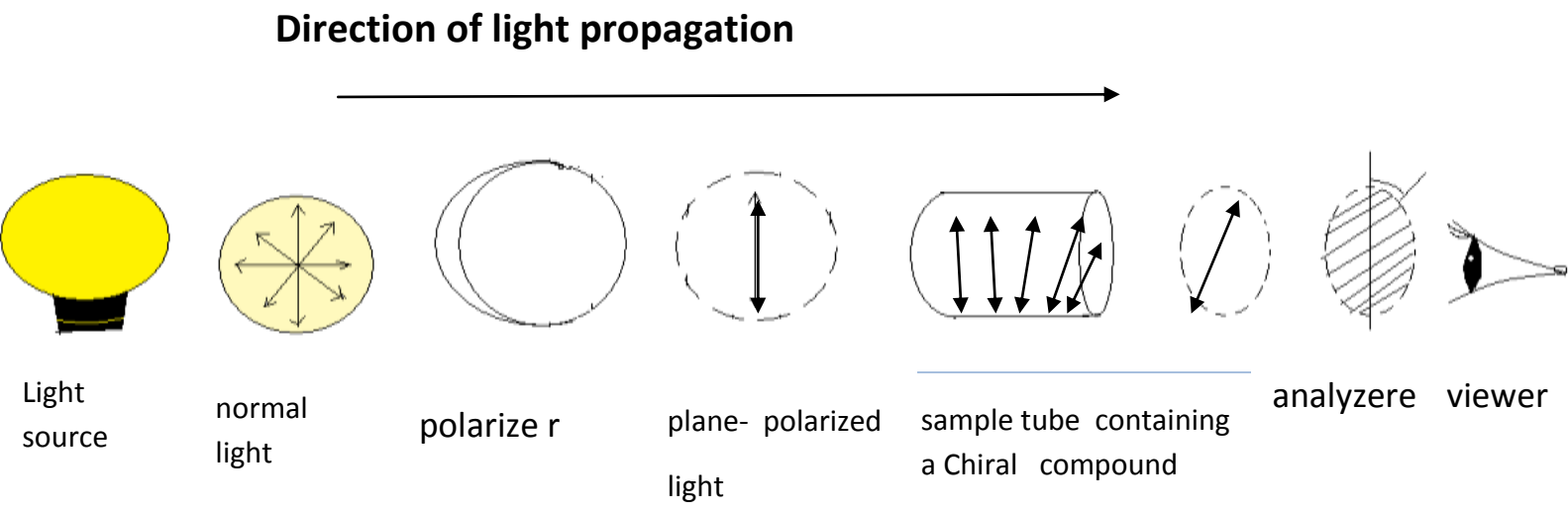
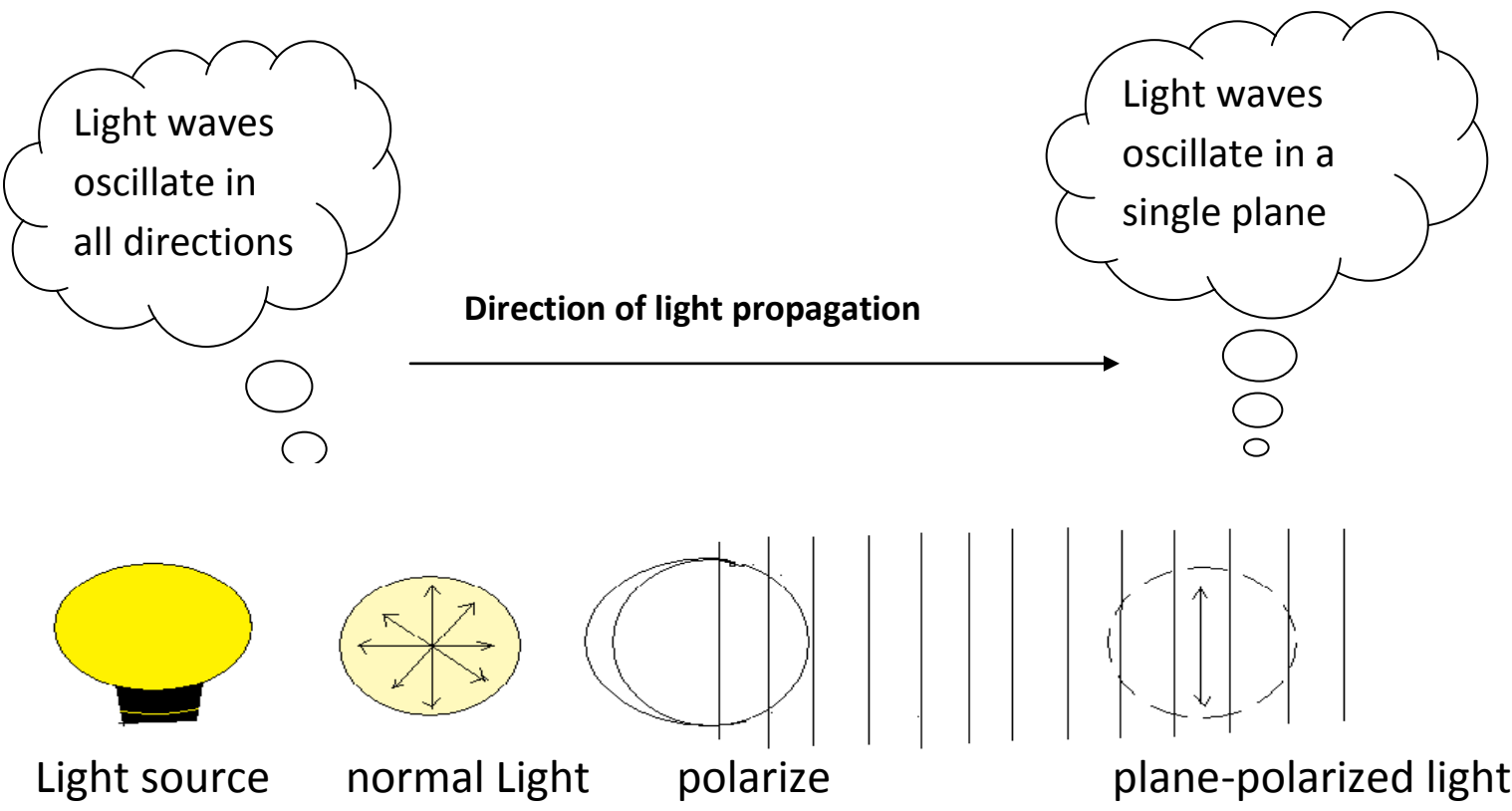
## **Optical isomerism**

### **Why optical isomers?**

optical isomers are named like this because of their effect on plane polarized light .

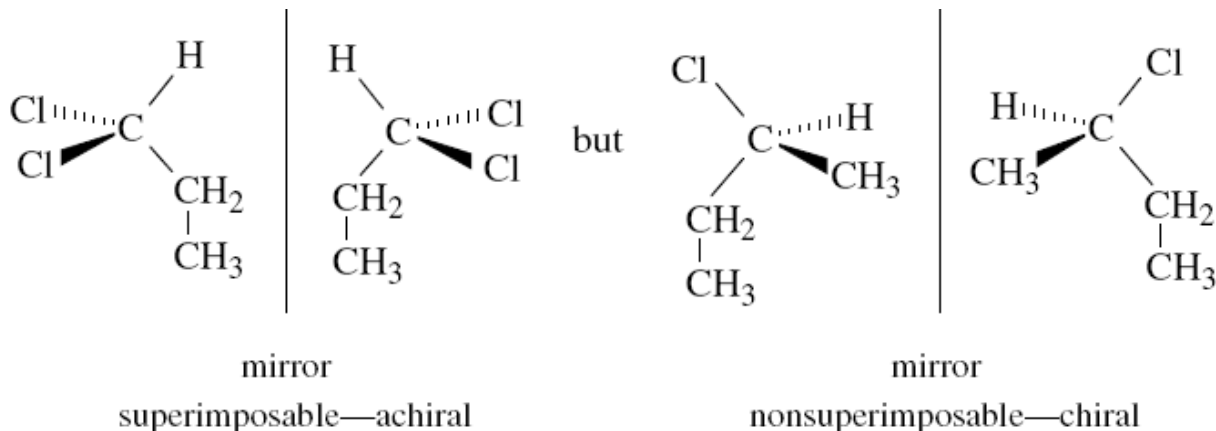
### **What is polarized light?**

Light is a wave motion that contains oscillating electric and magnetic fields. The electric field of ordinary light oscillates in all planes. However, it is possible to obtain light with an electric field that oscillates in only one plane. such light is called plane-polarized light **or simply polarized light.**



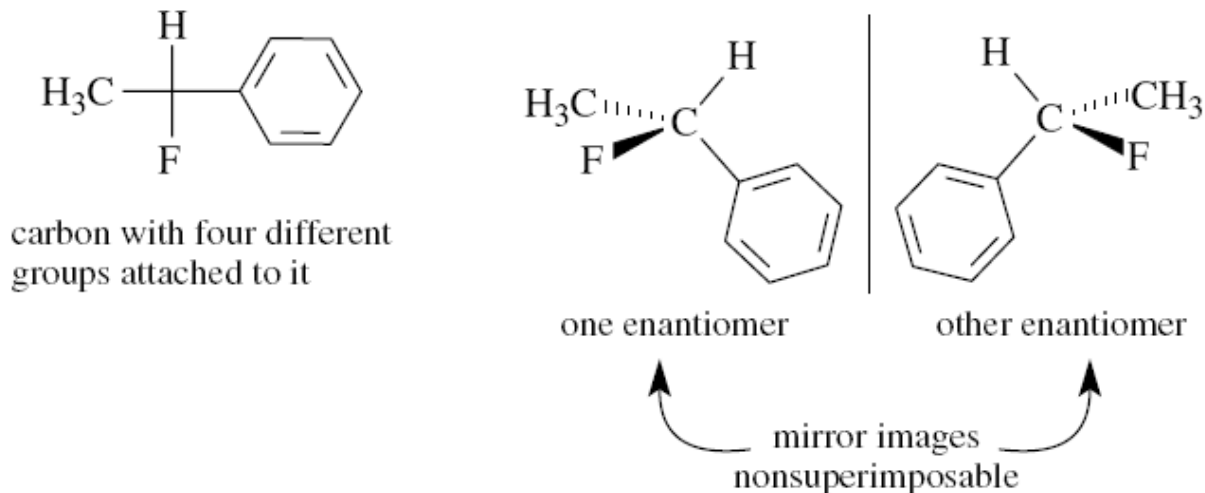
# Chirality:

Because of the tetrahedral geometry of saturated carbon and the associated three-dimensional properties, molecules can have chirality as one stereochemical feature. Any object is chiral if it is different (nonsuperimposable) than its mirror image. Likewise a molecule is chiral if it is nonsuperimposable on its mirror image. This requirement does not consider conformational changes (rotations about single bonds) as valid conditions for nonsuperimposability. Thus, for the molecules below, the first is achiral (not chiral) because it is superimposable on its mirror image and the second is chiral because it is not superimposable on its mirror image.



When a molecule is chiral, then it will have two isomeric forms called **enantiomers**, each of which is the nonsuperimposable mirror image of the other. Enantiomers are distinct stereoisomers because they are compounds that have the same molecular formula and sequence of bonded elements but which differ in the spatial arrangement of groups in the molecule. If a molecule is chiral, and thus has two enantiomers, it usually (but not always) contains at least one chiral center. In organic compounds a chiral center usually corresponds to an asymmetric tetrahedral carbon atom.





When trying to distinguish between chiral compounds, keep in mind the following:

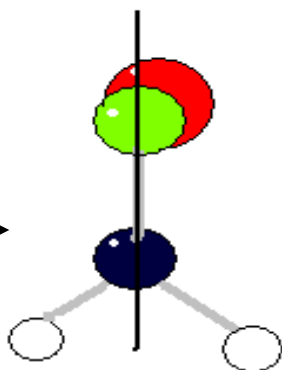
- Achiral molecules contain a plane of symmetry but chiral molecules do not.
- A plane of symmetry is a mirror plane that cuts a molecule in half, so that one half of the molecule is a reflection of the other half.

The achiral molecule  $\text{CH}_2\text{BrCl}$  has a plane of symmetry, but the chiral molecule  $\text{CHBrClF}$  does not.

$\text{CH}_2\text{BrCl}$   
Plane of symmetry

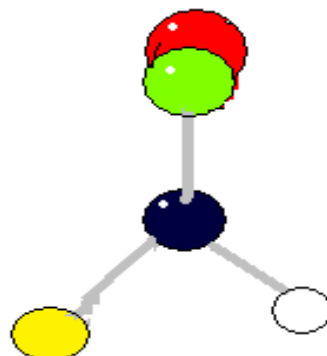
$\text{CHBrClF}$   
No Plane of symmetry

Aligning the C-Cl and  
C-Br bonds in each  
molecule.



This molecule has  
**two identical halves.**

$\text{CH}_2\text{BrCl}$  is achiral.



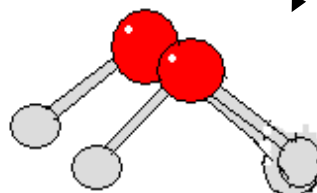
$\text{CHBrClF}$  is chiral.

$\text{H}_2\text{O}$

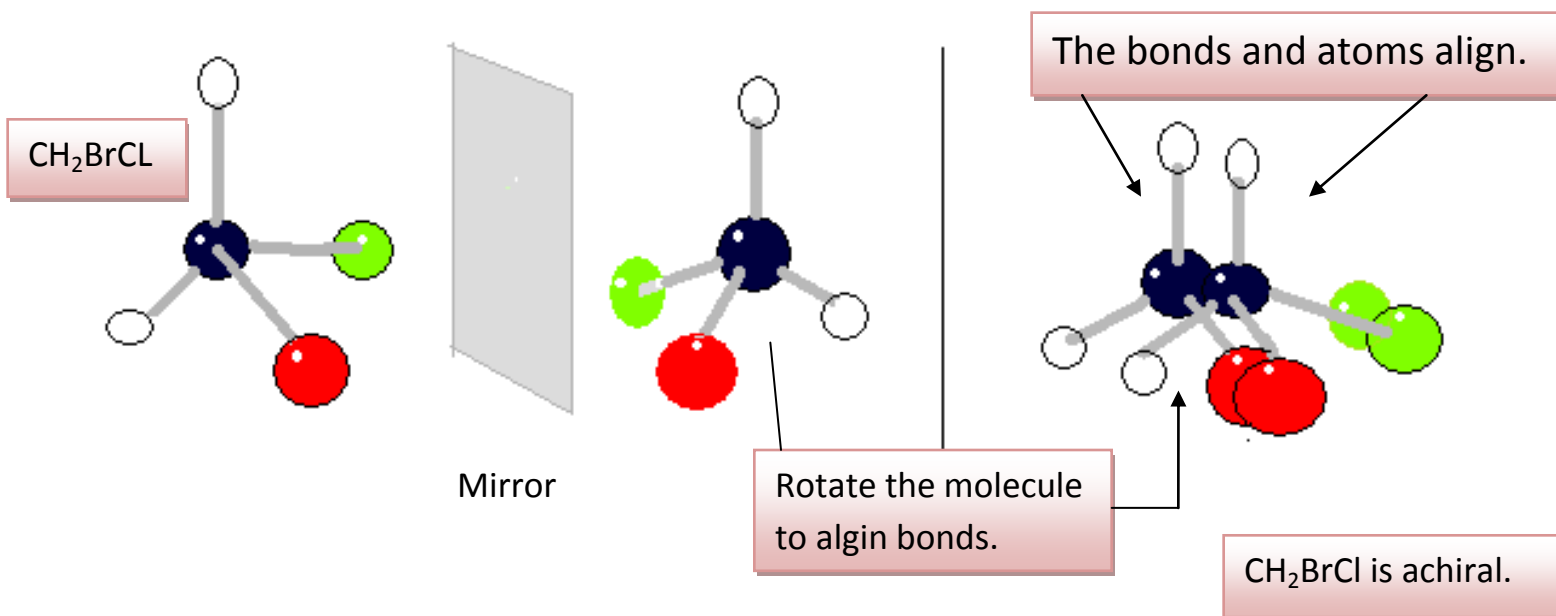


Mirror

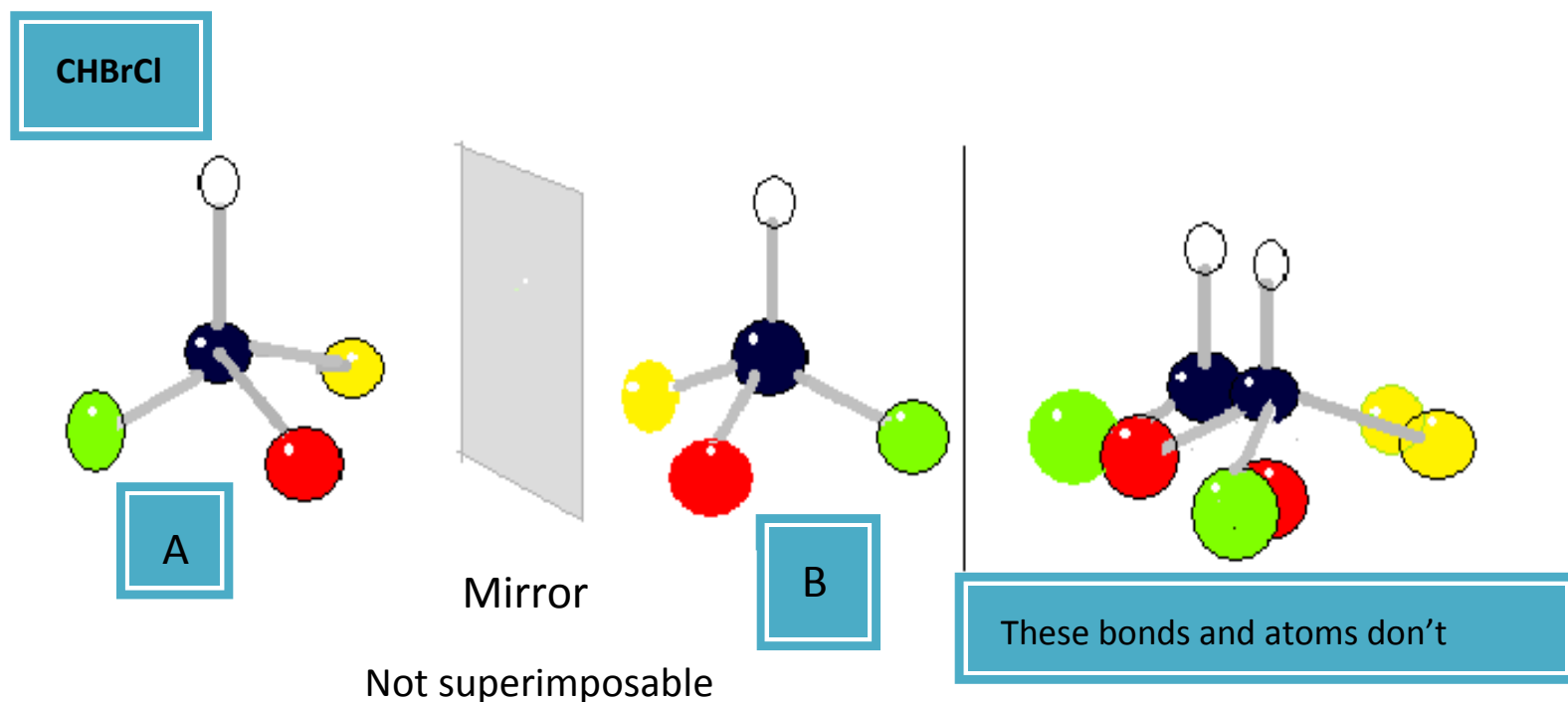
The bonds and atoms align.



$\text{H}_2\text{O}$  is achiral



With CHBrClF, the result is different. The molecule (labeled **A**) and its mirror image (labeled **B**) are not superimposable. No matter how you rotate **A** and **B**, all the atoms never align. CHBrClF is thus a **chiral molecule**, and **A** and **B** are different compounds.

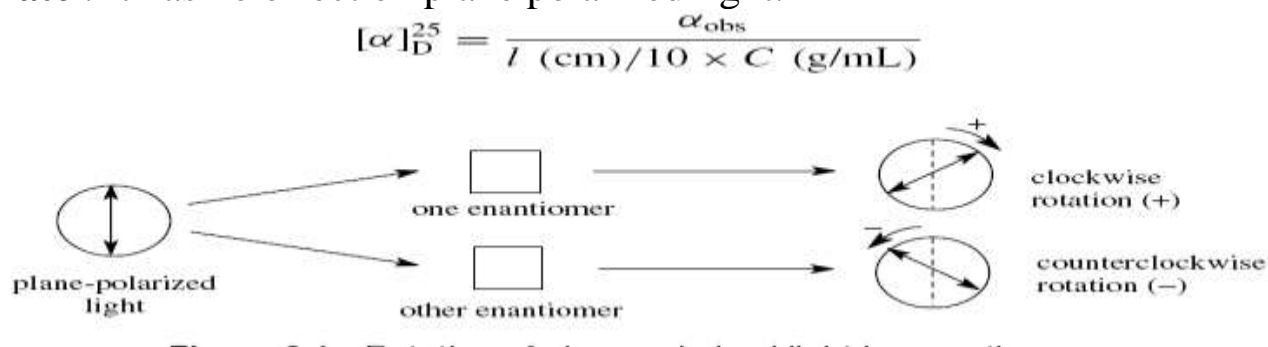


**A and B are stereoisomers** because they are isomers differing only in the three-dimensional arrangement of substituents. These stereoisomers are called **enantiomers**.

The recognition of chirality and chiral centers The four different groups attached to a chiral carbon can be different elements, isotopes, or functional groups, and chiral centers can be present in both in molecules is an important step in determining the numbers of stereoisomers that are possible for a given compound.

## Optical activity:

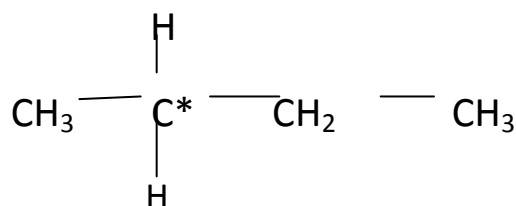
If a compound rotates plane-polarized light, it is termed **optically active**. To be optically active, a compound must be chiral and one enantiomer of the compound must be present in excess over its mirror image. The enantiomer which produces clockwise rotation of plane-polarized light is designated the positive enantiomer, and the enantiomer which produces counterclockwise rotation of plane-polarized light is designated the negative enantiomer. When optically active substances are made in the lab, they often occur as a 50/50 mixture of the two enantiomers. This is known as a **racemic mixture** or **racemate**. It has no effect on plane polarized light.



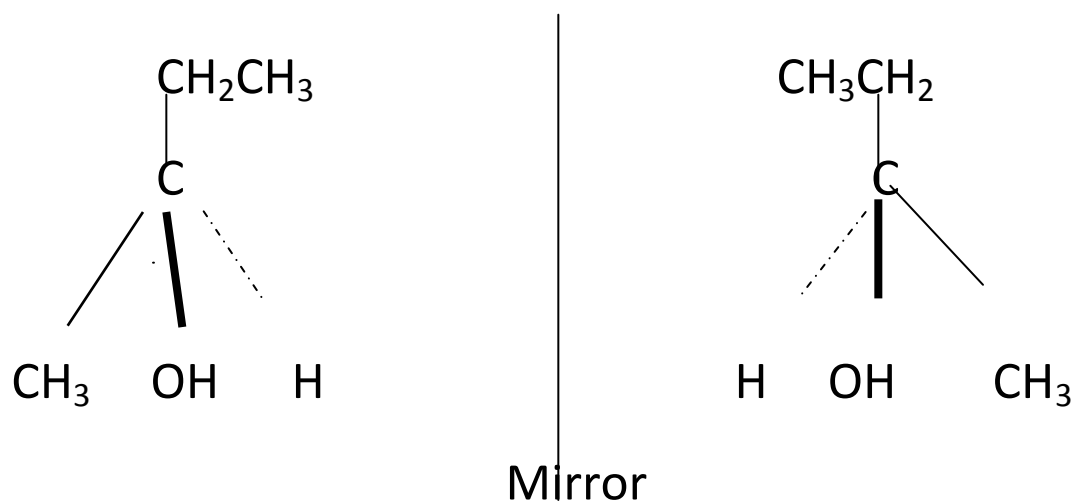
## Some real examples of optical isomers:

Butan -2-ol

The asymmetric carbon atom in a compound (the one with four different groups attached) is often shown by a star.



It's extremely important to draw the isomers correctly . Draw one of them using bond notation to show the 3-dimentional arrangement around the asymmetric carbon atom. Then draw the mirror to show the examiner that you know what you are doing ,and then the mirror image.

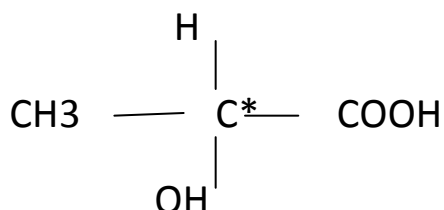


It doesn't matter in the last in what order you draw the four groups around the central carbon. As long as your mirror image is draw accurately, you will automatically have drawn the two isomers.

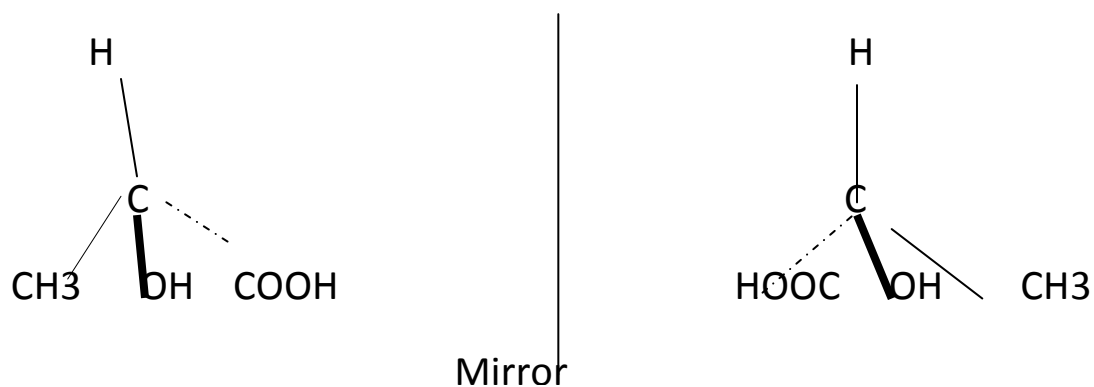
So which of these two isomers is (+) butan-2-ol and which is (-) butan-2-ol?

## 2-hydroxypropanoic acid (lactic acid)

Once again the chiral centre is shown by a star

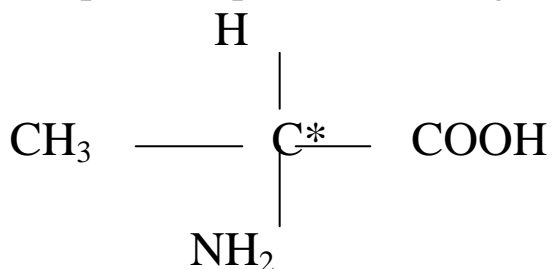


The two enantiomers are :

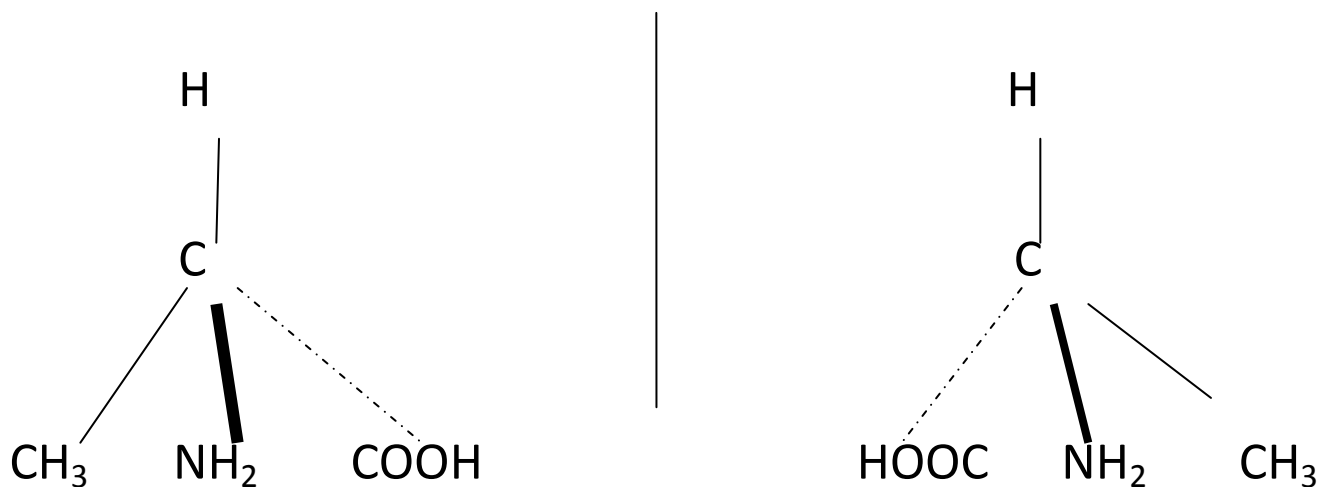


### 3-Aminopropanoic acid(alanine)

This is typical of naturally-occurring amino acids. Structurally, it is just like the last example, except that the -OH group is replaced by  $\text{-NH}_2$



The two enantiomers are:



Only one of these isomers occurs naturally: the (+) form. You can't tell just by looking at the structures which this is.

It has, however, been possible to work out which of these structures is which. Naturally occurring alanine is the right-hand structure is called **Dextrorotatory**, and the way the groups are arranged around the central carbon atom is known as an L-configuration is called **Levorotatory**. Notice the use of the capital L. the other configuration is known as **D**.

so you may well find alanine described as **L-(+) alanine**.

That means that it has this particular structure and rotates the plane of polarization clockwise.

## **Lec:2**

### *Resolution of Racemic Mixtures*

#### **Resolution:**

Is the process of separating a pair of enantiomers into the pure stereoisomers.

#### Methods of resolving racemic mixtures:

##### **1. Mechanical separation:**

Louis Pasteur first used this method in 1848 to separate the stereoisomers of a crystalline tartaric acid salt.

Separate solutions of the two separate isomers had the same specific rotation, but differed in the sign of rotation. This is a rather special method, which can't be applied to all racemic mixtures.

##### **2.Resolution using Diastereomers.**

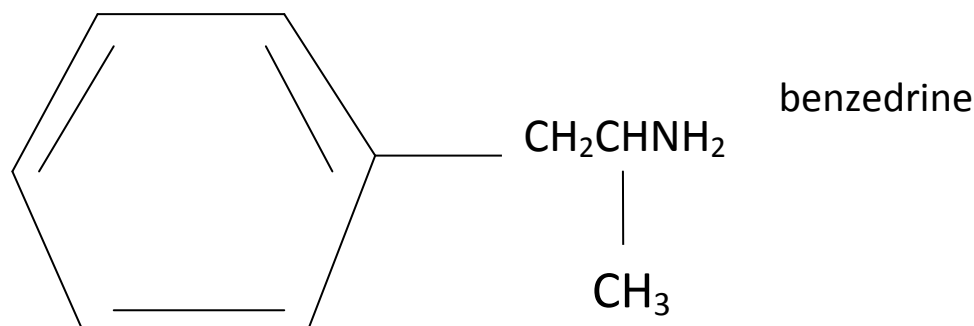
This method is based on the fact that diastereomers have different physical properties.

The method involves the followings:

- a.** the racemic mixture is reacted with an optically active reagent yielding a product which a mixture of two diastereomers.
- b.** according to a certain physical property (say their solubility in ethanol), the diastereomers are separated from one another.

c. the separated diastereomers are each reacted to reconvert them to the optically active reagent and the separated enantiomers.

Example : The stimulant Benzedrine:

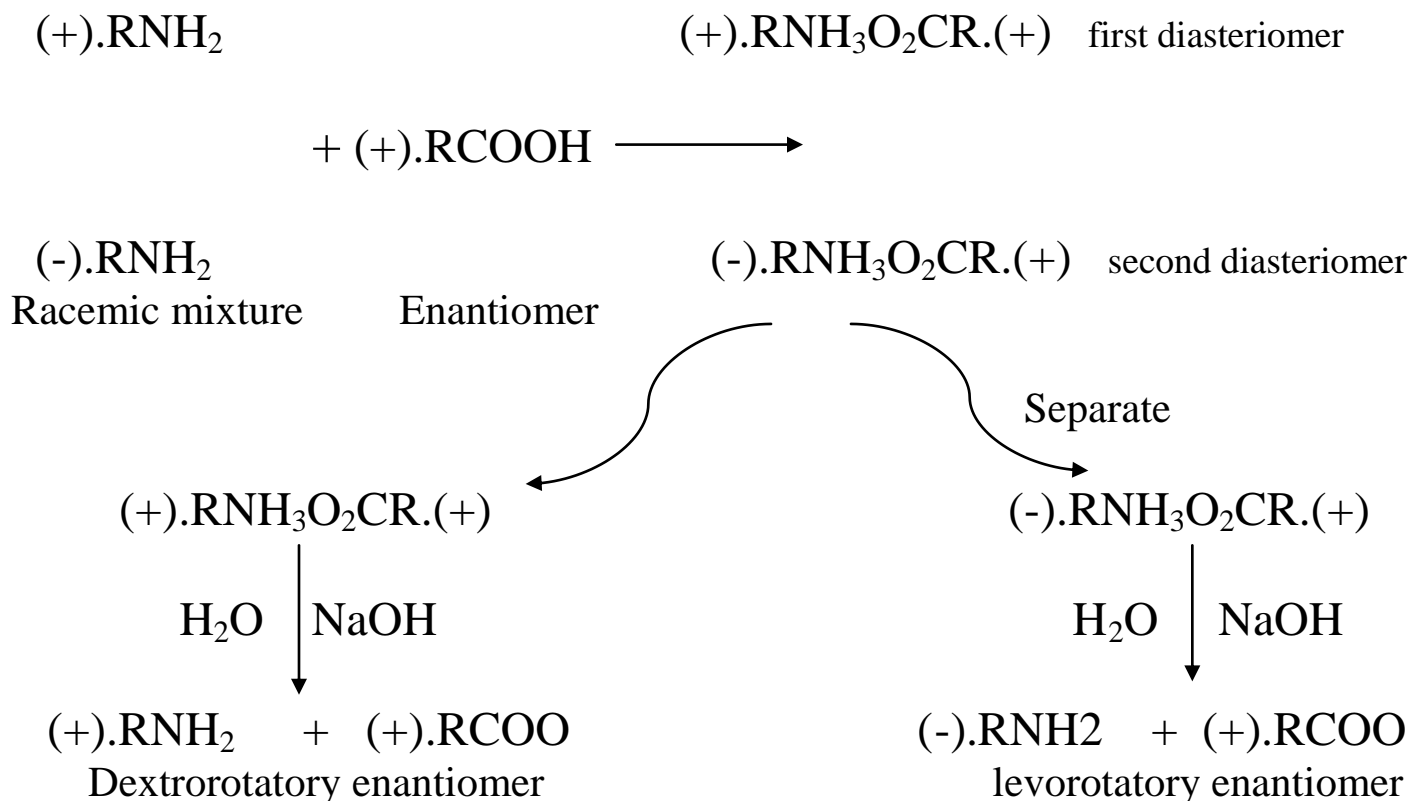


The functional group of Benzedrine is an amine group. It is a base that reacts with acids (organic or inorganic) to form salts. We can use an organic acid that is a pure enantiomer such as (+)-tartaric acid.

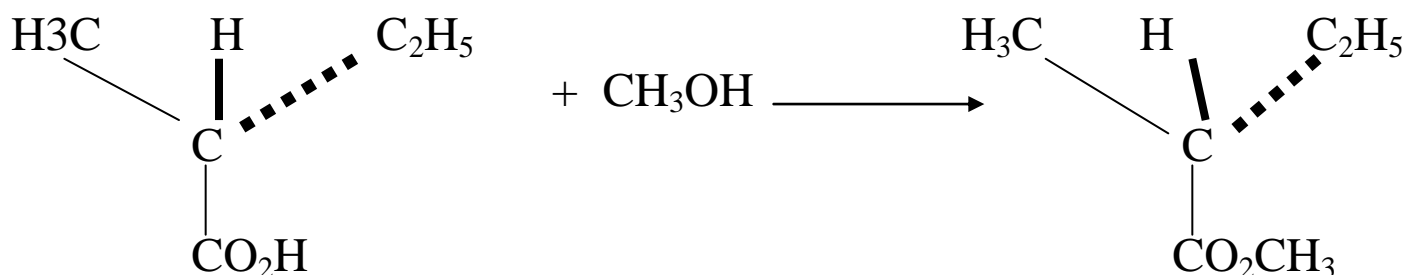
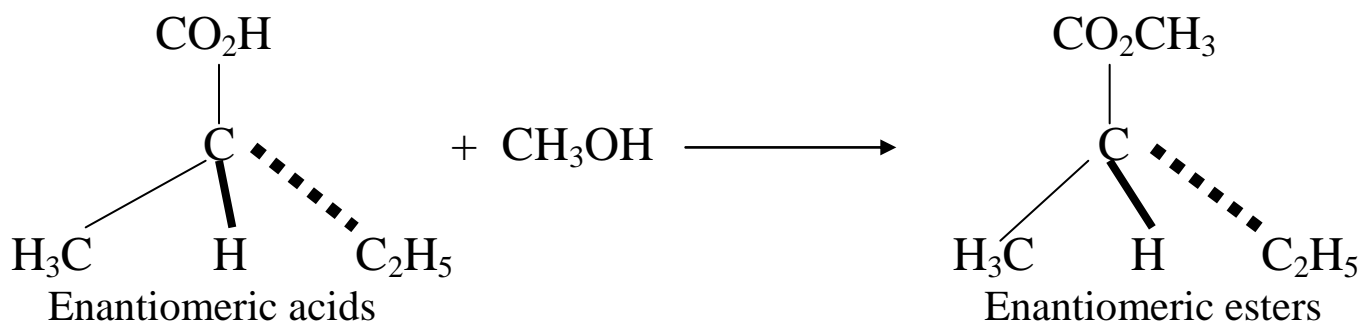
The acid reacts with racemic Benzedrine to form two diastereomeric salts.

Once the diastereomers are separated, Each can be reacted with an aqueous solution of sodium hydroxide to form one enantiomer of Benzedrine.

This is the most general technique for resolving racemic mixtures.

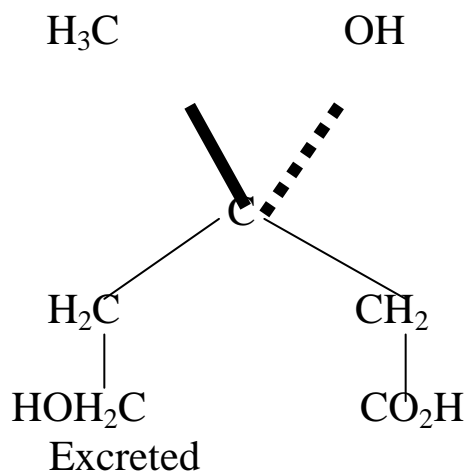
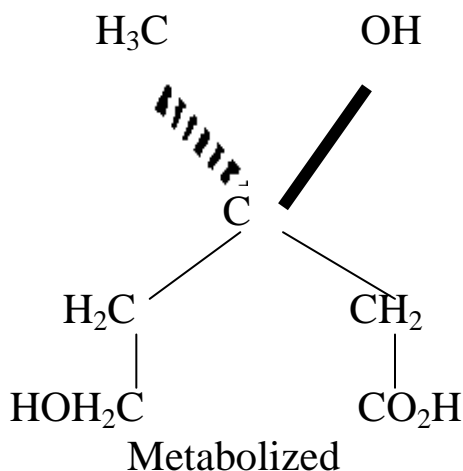






### 3. Enzymatic (Biological) resolution.

If a racemic mixture can be fed to a living organism, then it is often found that one enantiomer is preferentially metabolized. If this is so, then the unwanted isomer can sometimes be recovered. When a racemic mixture of mevalonic acid (3,5-dihydroxy-3-methylpentanoic acid) is fed to rats, one optical isomer is totally absorbed, and almost all the other is excreted in the urine, from which it can be recovered.



### Mevalonic acid

This method suffers from several disadvantages, compounds may be poisonous, and even if this method works, one of the enantiomers is always lost.

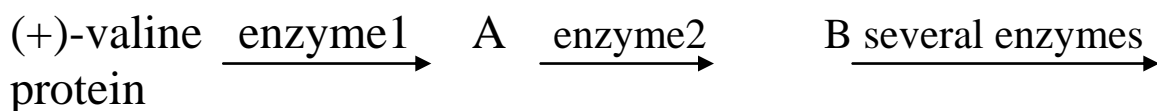
## Chiral compounds and living systems:

a pair of enantiomers will react different only with chiral reagents. Because living systems usually react with only one of a pair of enantiomers, the living system is also chiral.

The part of the living system that is chiral is the enzyme. An enzyme has the ability to react with only one of a pair of enantiomers. This ability of an enzyme is called its **stereospecificity**

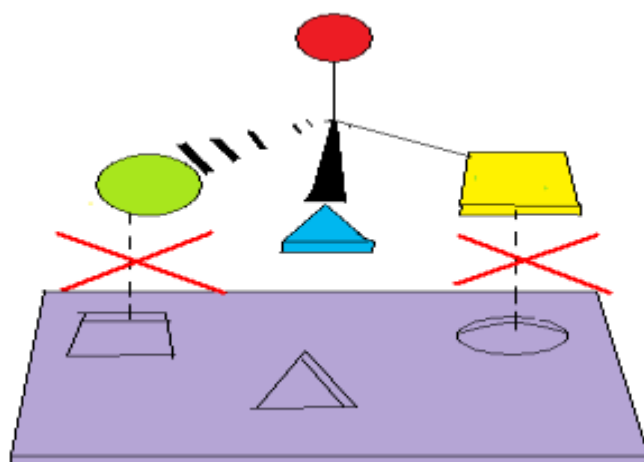
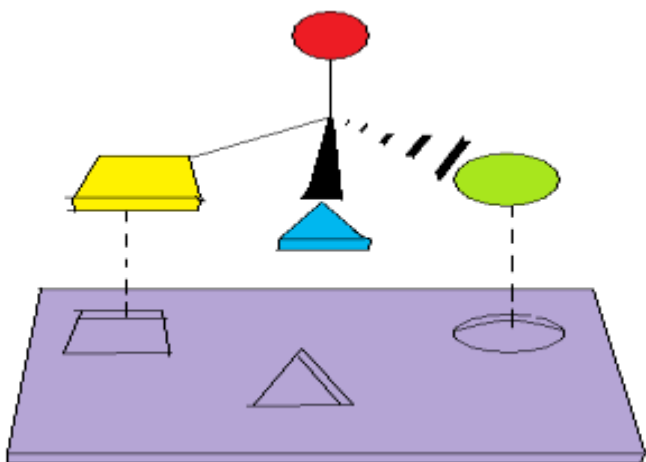
For example :

- ❖ Our bodies convert (+) -valine, an amino acid, along with other amino acids into proteins necessary for our growth and development. However, (-)-valine is not employed at all.



R enantiomer

S enantiomer



Binding site of the receptor

binding site of the receptor

- ❖ (+) -Amphetamine excites the central nervous system in humans three to four times more than (-) amphetamine.
- ❖ (-)-Ascorbic acid (vitamin) prevents scurvy, while (+)-Ascorbic acid does not.

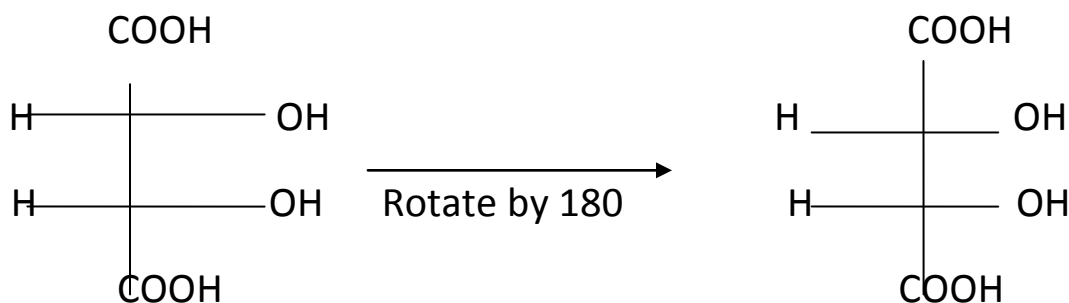
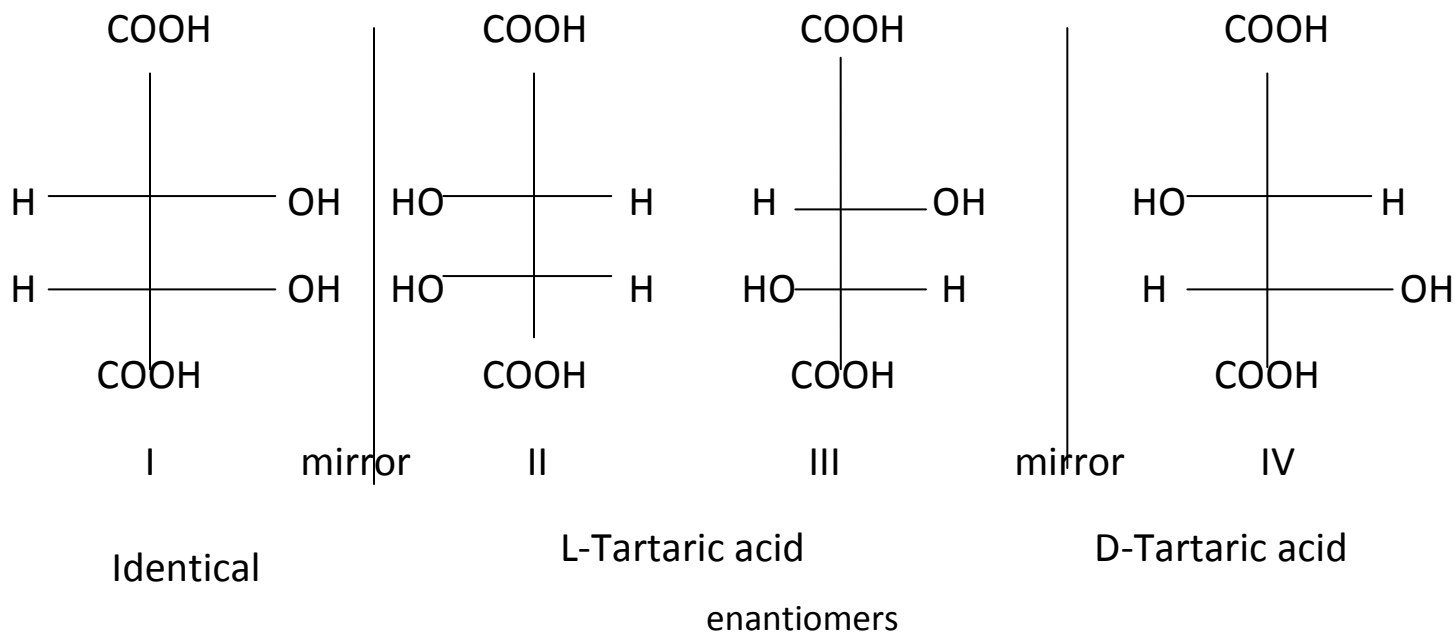
# Stereoisomerism in Compounds with two similar chiral Centers (MESO compound)

A meso compound: is one whose molecules are superimposable on their mirror images even though they contain chiral centers.

## Examples:

### 1. Tartaric acid $\text{HOOC}\text{C}^*\text{H}(\text{OH})\text{C}^*\text{H}(\text{OH})\text{COOH}$

It has two chiral atoms, so, four stereoisomers would be expected



Identical to II

The term meso is given to an isomer that contains chiral atoms but can be superimposed on its mirror image.

Because of this a meso stereoisomer is optically inactive. Therefore there are only three stereoisomers of tartaric acid: a meso isomer and a pair of enantiomers.

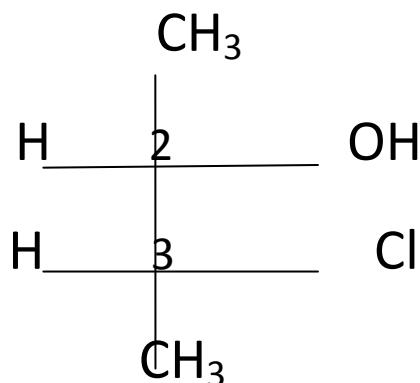
The meso form like the racemic mixture exhibits physical properties that differ from those of the enantiomers.

### ***Stereoisomerism in compounds with two or more dissimilar Chiral centers*** **( Diastereomers)**

Two dissimilar chiral centers are carbons that differ in at least one bonded group.

Examples:

1. ) 3-chloro-2-butanol:



Chiral carbon 2 is linked to -H, CH<sub>3</sub>, -OH, and -CH(Cl)CH<sub>3</sub>.

Chiral carbon 3 is linked to -H, CH<sub>3</sub>, -Cl, and -CH(OH)CH<sub>3</sub>.

Two of the groups bonded to each chiral center are the same (-H, CH<sub>3</sub>) But the two other groups bonded to each chiral carbon differ (-OH versus Cl) and (-CH(Cl)CH<sub>3</sub> versus -CH(OH)CH<sub>3</sub>). these chiral carbons are dissimilar.

**The number of optically active stereoisomers of a molecule with two or more dissimilar chiral carbons can be calculated using the following expression, known as van't Hoff's rule:**

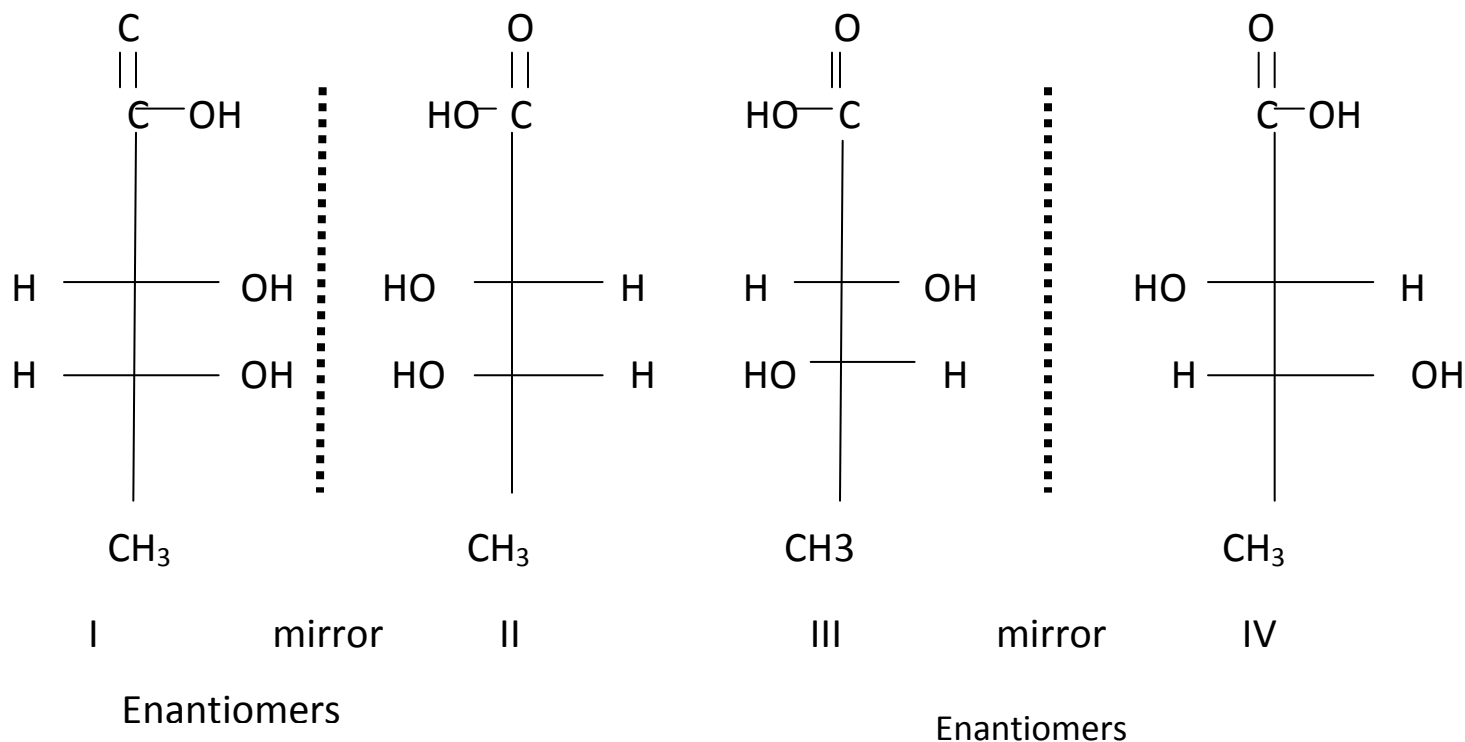
## Number of stereoisomers=2<sup>n</sup>

**n** represents the number of dissimilar chiral centers in the molecule.

♣ Applying this rule on the previous example (3-chloro-2-butanol) shows that it can exist as four possible stereoisomers ( $2^2=4$ ).

2. ) **2,3-dihydroxybutanoic acid** [**HOCC\*H(OH)C\*H(OH)CH<sub>3</sub>**].

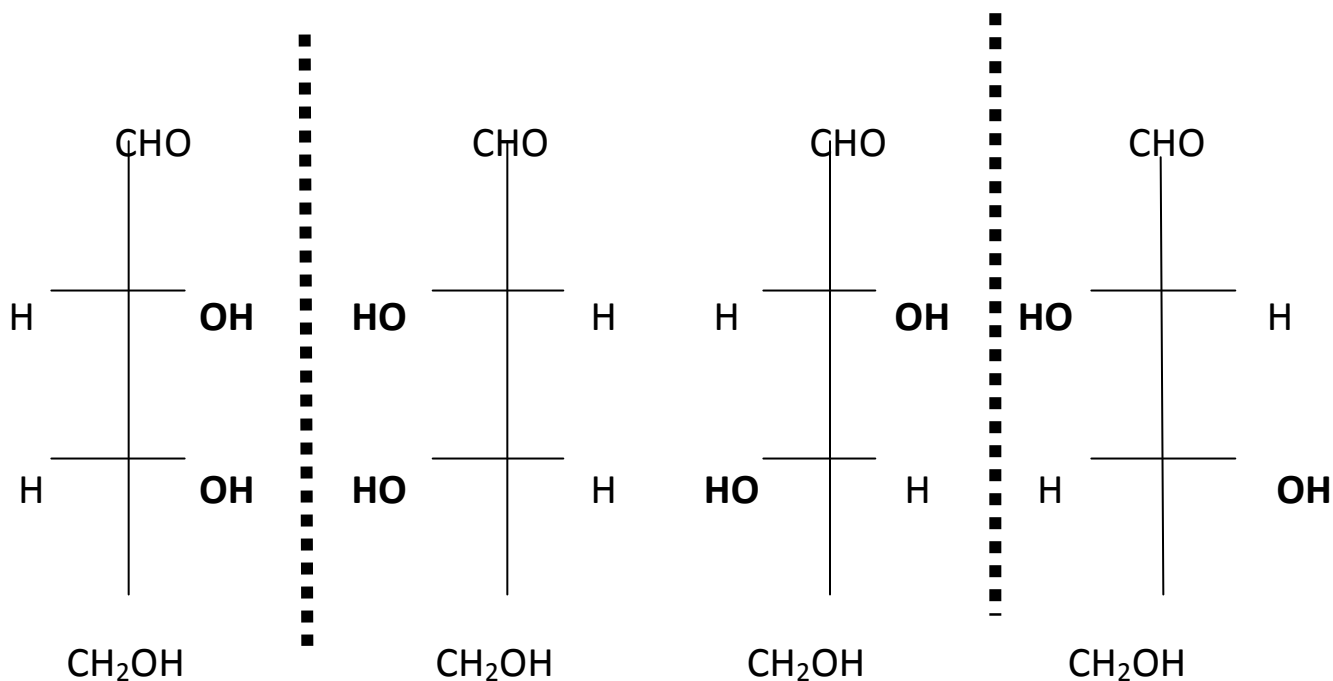
A structure with two dissimilar chiral carbons, it can exist as four possible stereoisomers (applying van't Hoff's rule).



Stereoisomers that are not enantiomers are diastereomers .Thus:

Structures I and III,  
Structures I and IV,  
Structures II and III,  
Structures II and IV, } are diastereomers

3. )2,3,4-Trihydroxybutylaldehyde[HOCH<sub>2</sub>C\*H(OH)C\*H(OH)CHO] ,  
a structure with two dissimilar chiral carbons, it can exist as four possible  
stereoisomers (applying van't Hoff's rule).



I mirror II  
Erythrose Enantiomer

III mirror IV  
Threose Enantiomers

Both are very soluble in ethanol

Both are slightly soluble in ethanol

Compound II is liquid

compound IV is solid m.p 132 °C

Structures I and II are enantiomers.

Structures III and IV are enantiomers.

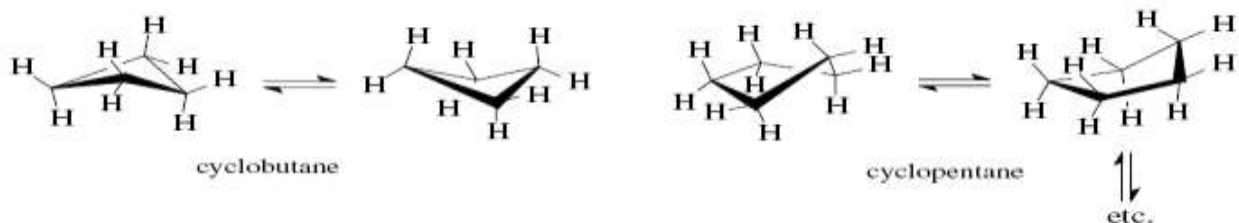
Stereoisomers that are not enantiomers are diastereomers thus:

Structures I and III,  
Structures I and IV,  
Structures II and III,  
Structures II and IV, } are diastereomers

## How do the properties of diastereomers compare?

1. **Diastereomers have similar chemical properties** because they are members of the same family. However, their chemical properties are not identical.
2. **Diastereomers have different physical properties:** different melting points, solubility's in a given solvent, densities, refractive indexes, and so on. Diastereomers differ in specific rotation, they may have the same or opposite signs of rotation, or some may be inactive. As a result of their differences in boiling point and in solubility, they can be separated from each other by fractional distillation or fractional crystallization; as a result of differences in molecular shape and polarity, they differ in adsorption and can be separated by chromatography.

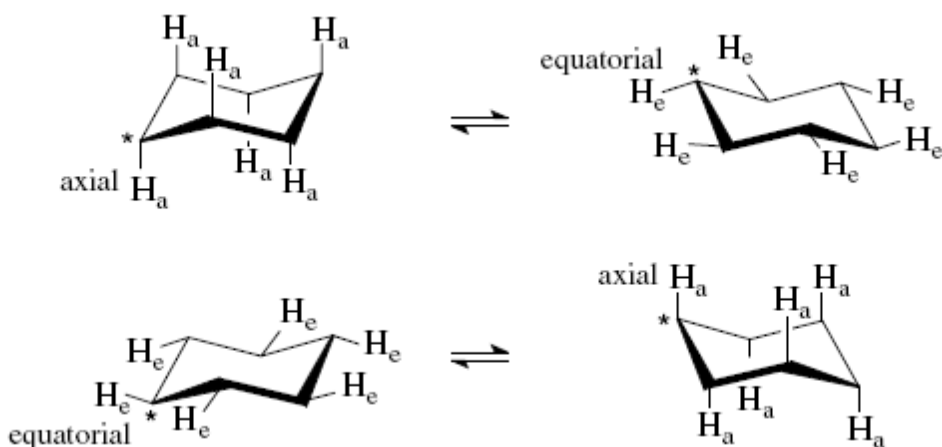
### The Stereochemistry Of Cyclic System



---

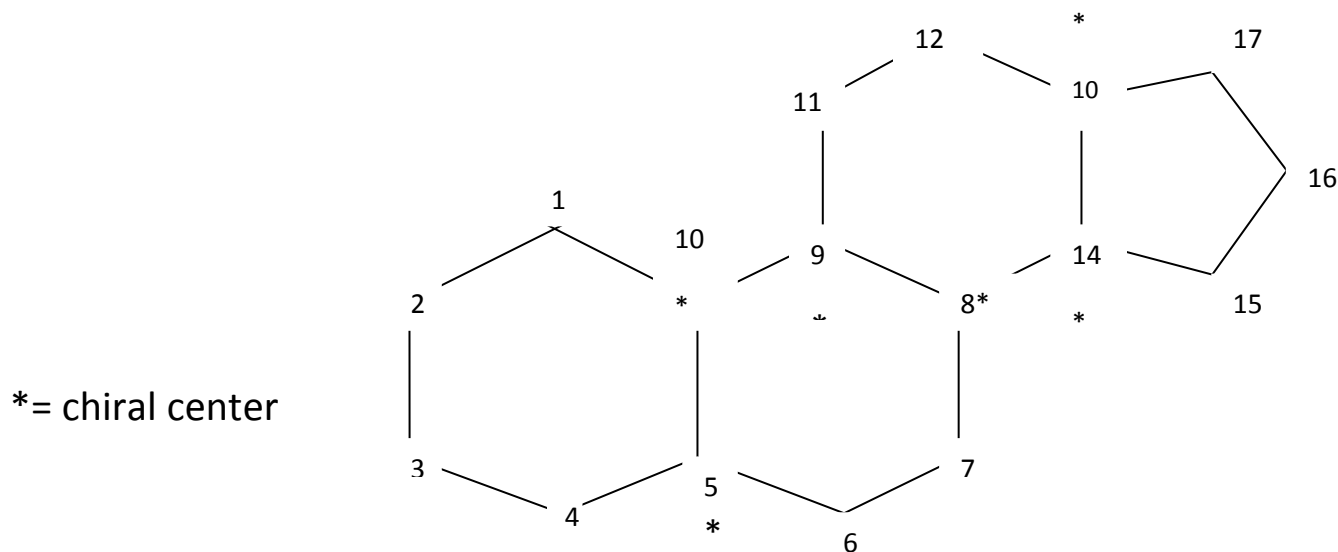
*The boat form is not important in practice.*

In the chair form two different types of C-H bond can be shown, differing in their orientation with respect to the plane of the ring and described as “axial” and “equatorial”.



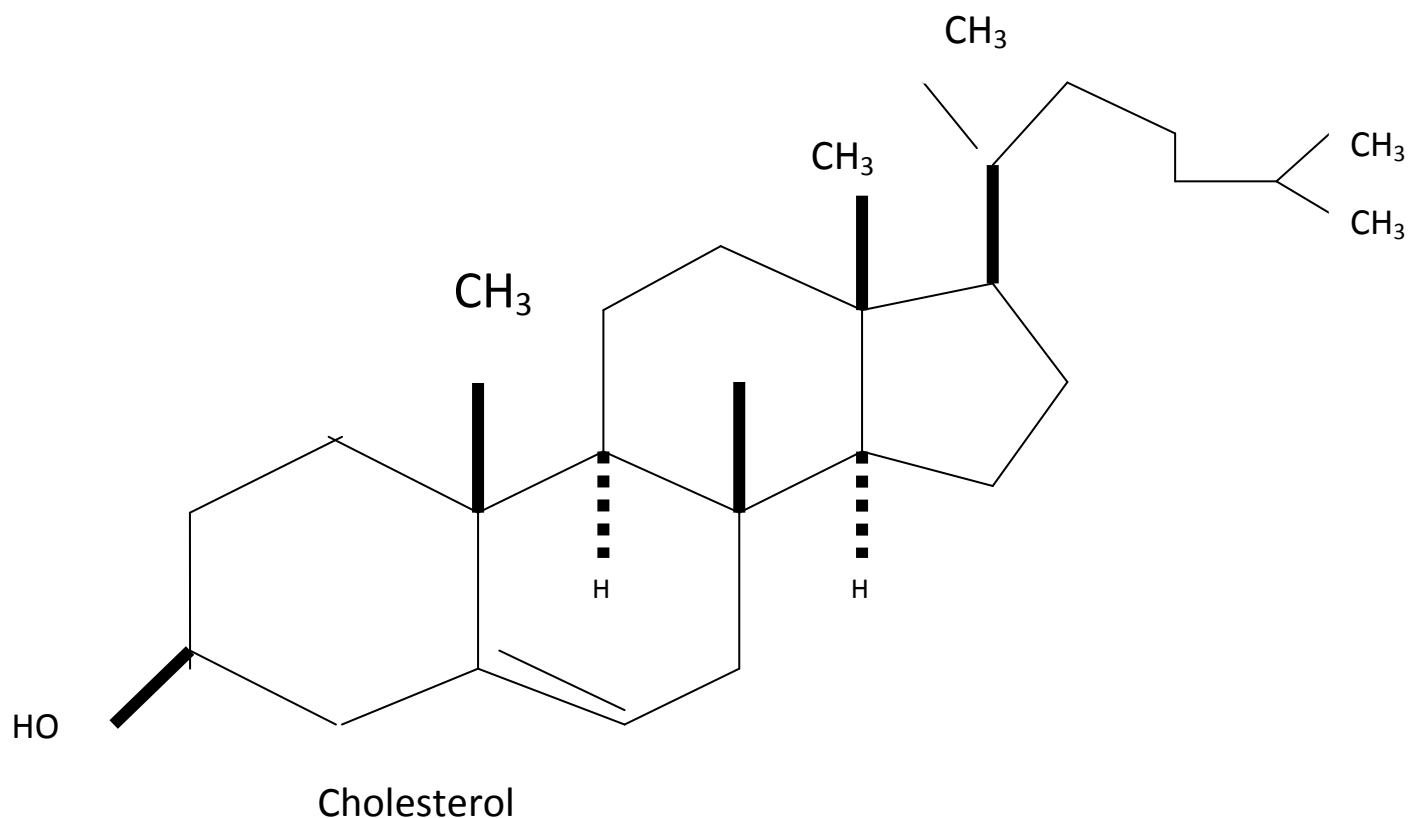
### **Steroids:**

The steroids are a group of polycyclic aliphatic compounds derived from the saturated tetracyclic system:



**Cholesterol:** is one of the most important physiologically active steroid.

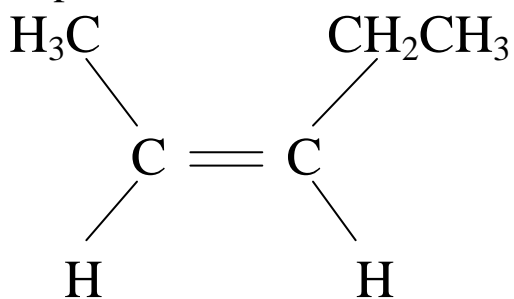




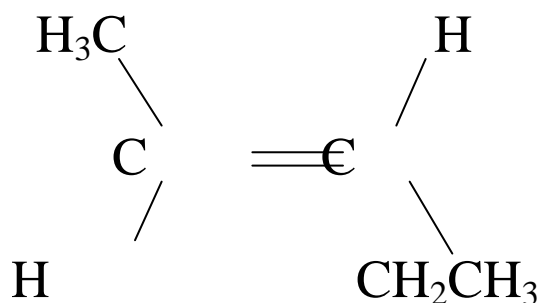
Bile acids: are steroidal carboxylic acids. These compounds assist the digestive process by emulsification of fats in the intestine i.e. they are intestinal detergents.

### Cis-trans isomers

**Configurational isomers** cannot interconvert because the double bond cannot rotate, cyclic compounds can also have cis and trans isomers because the cyclic system prevents free rotation about the single bonds.



Cis-2-pentene



trans-2-pentene